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Comparing the Effect of Fluoxetine and Escitalopram on Inflammation and Glycemic Control in Patients Having Psychiatric Illness with Type 2 Diabetes Mellitus

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Keywords: Psychiatric illness, Type 2 Diabetes Mellitus, C-Reactive Protein, Fasting Blood Sugar, Fluoxetine, Escitalopram.

ABSTRACT

Background: Diabetes and Psychiatric disorders influence each other in multiple ways. This can, in turn, result in elevated C - reactive protein, which acts as a biomarker of inflammation, thereby increasing the risk of Cardio-Vascular Diseases. Several research suggests a bidirectional relationship between Type 2 Diabetes Mellitus (T2DM) and Psychiatric illness & the two disorders may share similar pathophysiological mechanisms. Objective: To compare the two anti-depressants, Fluoxetine and Escitalopram on their effectiveness in reducing C-reactive Protein and Fasting Blood Sugar in Patients with Psychiatric illness and Type 2 Diabetes Mellitus. Methods: A prospective study was conducted in the Department of Psychiatry at Pushpagiri Medical College Hospital. Newly diagnosed patients with Psychiatric illness and already diabetic were selected. The study period was 6 months and follow-up was taken four weeks of initiating either Escitalopram (10mg) or Fluoxetine (80mg) for Psychiatric illness. Results: The percentage reduction in both C-reactive Protein and Fasting Blood Sugar were calculated and it was found to be statistically significant with $p<0.05$. Escitalopram group showed a significant reduction in both C - reactive protein and Fasting Blood Sugar values after four weeks of therapy.Conclusion: The results imply that use of Escitalopram can reduce the chance of cardiovascular events by reducing the CRP levels. Thus, based on the results, Escitalopram may be considered as the treatment of choice in patients having a Psychiatric illness with comorbid Type 2 Diabetes.

INTRODUCTION

Psychiatric disorders have been considered as "mental" rather than as the physical illness. This is because they manifest with disorder functioning in the area of emotion, perception, thinking, and memory. The types include Stress-related disorders, Anxiety disorders, Affective disorders, Schizophrenia and Delusional disorders, Substance misuse disorder, Organic disorder, Disorders of adult personality and behavior, Eating disorders, Somatoform disorders, Neurasthenia, Puerperal mental disorder. The etiology of psychiatric disorders is multifactorial with a combination of biological factors (Genetic factors, Brain structure, and function); Psychological and behavioral factors (Early environment, Personality and Behavior) and social causes (Social isolation and Stressors).[1]

C-reactive protein, it is a sensitive systemic marker of inflammation and tissue damage and is produced by hepatocytes predominantly under transcriptional control by the proinflammatory cytokine interleukin 6. Major depression has been shown to be associated with activation of the inflammatory response. These changes include increased numbers of peripheral leucocytes, both monocytes, and neutrophils. Positive acute-phase proteins (including C-reactive protein) are increased.

Stress can result in inflammation in predisposed individuals that can, in turn, lead to the activation of indolamine 2,3 dioxygenase pathway and thus reduces serotonin availability and increased glutamate receptor activation leading to Major Depressive Disorder.

Current research suggests a bidirectional relationship between Type 2 Diabetes Mellitus (T2DM) & depression & the two disorders may share similar pathophysiological mechanisms [14]. Depression was associated with a 60% increase of type 2 diabetes while type 2 diabetes was only associated with a moderate (15%) risk of depression [15]. On one side, depression could facilitate the onset of diabetes through disturbances in eating behaviors, increase in potentially damaging behaviors (smoking and alcohol consumption), drug-induced weight gain, decreased self-care activities or activation of stress-related hormonal pathways (stimulation of the hypothalamic pituitary adrenal (HPA) axis, resulting in increased cortisol levels and a resulting increase in blood glucose, eventually progressing to diabetes) and pro-inflammatory cytokines which interfere with glucose metabolism[16]. On the other hand, limitations on diet and physical and social activities determined by diabetes, together with some diabetes-related symptoms (e.g., fatigue induced by hyperglycemia), could induce

depressed mood[17].The recognition of depression becomes important as cost-effective treatment is available resulting in improvement of diabetic care as well. In addition, few studies have evaluated the impact of specific antidepressant therapies on glycemic control in people with diabetes and fewer still have examined the incidence of new-onset diabetes among those treated for depression. Depression can lead to diabetes via insulin resistance through the activation of Hypothalamus Pituitary-Adrenal Axis and Sympathetic Nervous System. [5]Antidepressants are medicines that treat depression. They may help improve the way the brain uses certain chemicals that control mood or stress.

Fluoxetine belongs to Selective Serotonin Reuptake Inhibitor class and it acts by inhibiting the 5HT (hydroxytryptamine) receptor, which leads to an increase of serotonin level. It antagonizes muscarinic, histaminergic, and α1–adrenergic receptors, which lead to various anticholinergic, sedative actions. It is the longest acting SSRI and the plasma half-life is 2 days.

Escitalopram is the stereoisomer of Citalopram and is used in Major depressive disorder (MDD) and generalized anxiety disorder (GAD).It is a potent and selective inhibitor of central neuronal serotonin reuptake with little to no effect on nor epinephrine or dopamine reuptake. [3],[7]

MATERIALS AND METHODS

We conducted a prospective experimental study after getting approval from the Institutional Ethics Committee. The selection of patients was based on the inclusion and exclusion criteria.

INCLUSION CRITERIA

- IP/OP patients.
- Both male and female patients.
- Those who are able to give informed consent.
- Patients newly diagnosed with Psychiatric illness and existing Type 2 Diabetes Mellitus
- Patients starting antidepressant medication, either ESCITALOPRAM (10mg) or FLUOXETINE (80mg)

- Patients on Oral Hypoglycemics (Metformin 500mg) for glycemic control
- Patients of age : > 18 years

EXCLUSION CRITERIA

- Pediatric patients.
- Pregnant women.
- Patients with co-morbidities other than Diabetes
- Patients on Insulin and hypoglycemic agents other than Metformin
- Those who are unable to give informed consent.

Informed consent was taken from each selected patients prior to the initiation of the study. Patient's data collection form was used for recording the demographic details of the patients. The study period was 6 months and follow-up was taken four weeks of initiating either Escitalopram (10mg) or Fluoxetine (80mg) for Psychiatric illness. For the determination of parameters like FBS and CRP, the residual blood was collected from the laboratory and determined using semi-auto analyzer in Pushpagiri College of Pharmacy. These parameters were determined before initiating the specific anti-depressants and after four weeks of initiating the anti-depressant medication.

Statistical Analysis

Data were analyzed using Microsoft Excel 2007 and Statistical Package for Social Sciences (SPSS).Paired t test was done to compare two different observations of a single parameter. The two different observations were before and after treatment values of CRP and FBS respectively. $p<0.05$ considered as statistically significant.

RESULTS

In the 6-month study, 70 psychiatric patients were enrolled as per inclusion and exclusion criteria. The patients were considered from OP and IP Department of Psychiatry.

The CRP levels of the patients, before and after (4 weeks) therapy were taken and the percentage reduction in CRP of Escitalopram and Fluoxetine group were calculated and both

the differences were statistically significant with a p value <0.05 using the paired t-test. Comparatively, Escitalopram group showed slightly greater significance than the Fluoxetine group in reducing the CRP

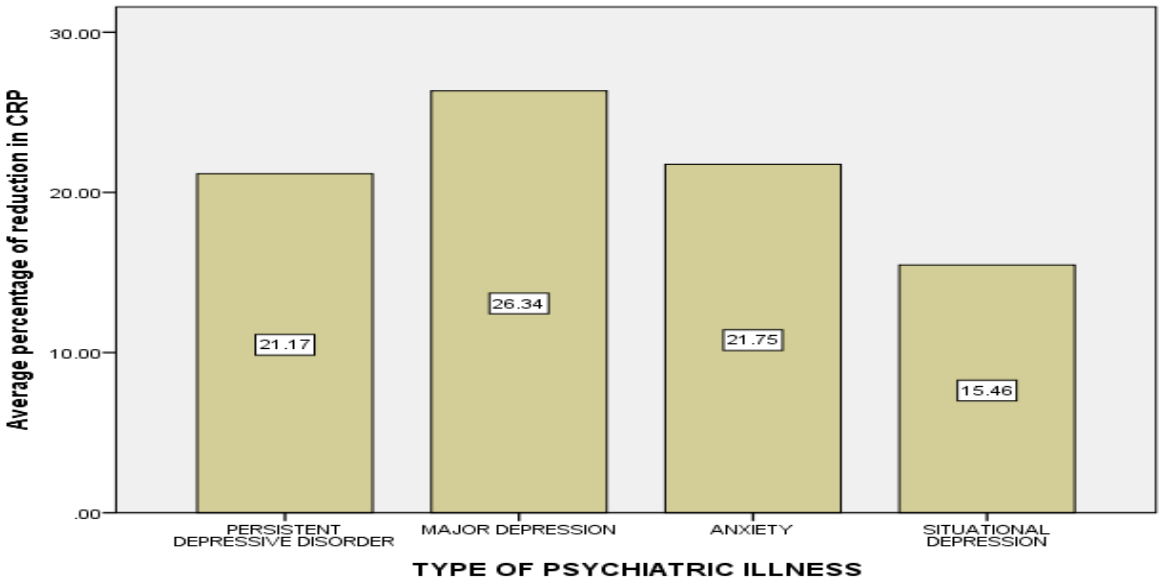

Figure 1: Average % reduction in CRP (Escitalopram group) based on the type of psychiatric illness.

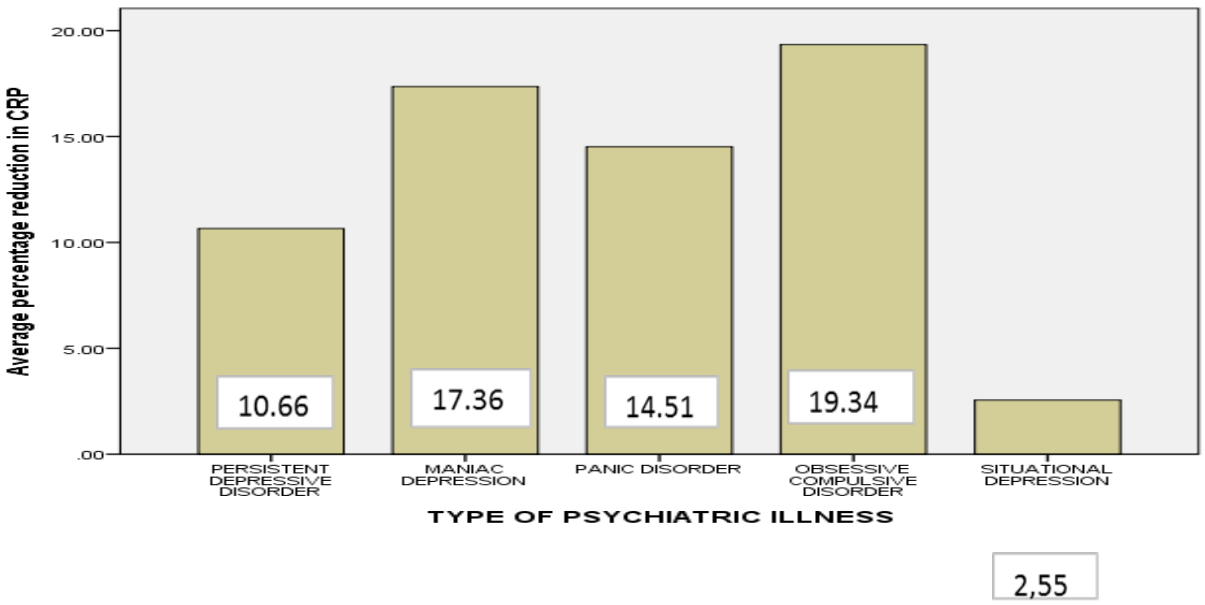

Figure 2: Average % reduction in CRP (Fluoxetine group) based on type of psychiatric illness

The FBS levels of the patients, before and after (4 weeks) therapy was taken and percentage reduction in FBS of Escitalopram and Fluoxetine group were found to be 11.25 and 2.94 respectively and both the differences were statistically significant with a p <0.05 using a paired t-test. Comparatively, Escitalopram group showed slightly greater significance than the Fluoxetine group in reducing the FBS.

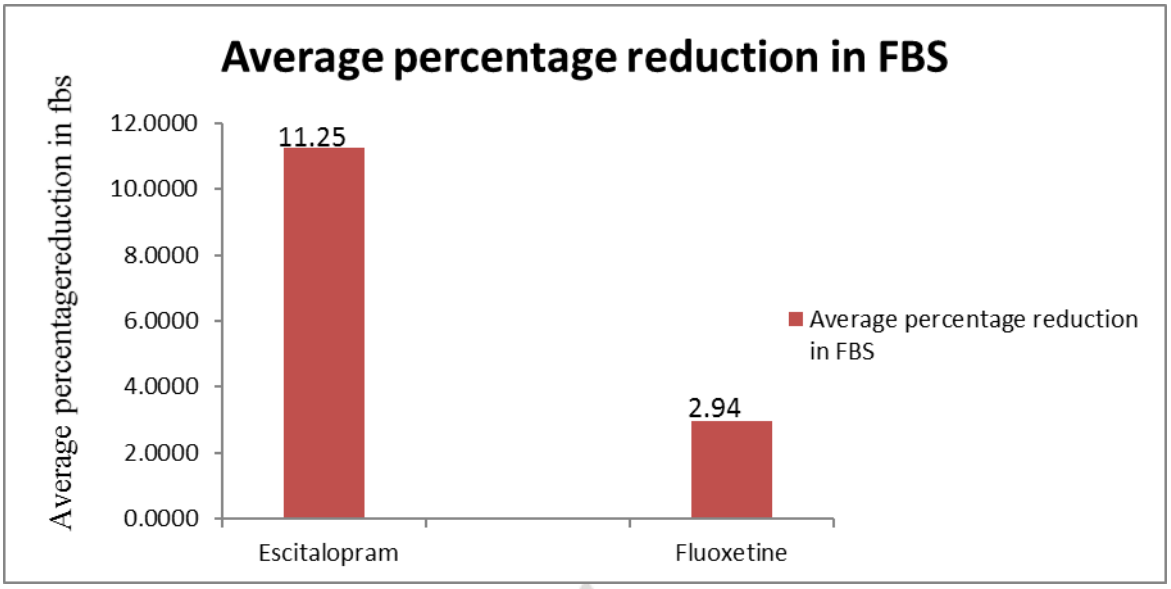

Figure 3: Comparison of the average percentage reduction in FBS in both Escitalopram and Fluoxetine group

The patients involved in the study belonged to the 30-80 age group in which patients with age group 40-50 were large in number for both Escitalopram group and Fluoxetine group. Females were predominant in the study population than males.

Medication adherence of each patient was determined using Medication Adherence Rating Scale questionnaire(MARS). Proper counselling was given to the patient caregiver during the first consultation itself regarding the importance of medication adherence. The adherence was determined during follow-up(after four weeks of therapy).From the data obtained and it was found that majority adherence was shown by age group 45-80 in patients receiving Escitalopram and age group 46-60 showed high adherence in patients receiving Fluoxetine.

Quality of Life was also measured using Quality of Life Enjoyment and Satisfaction Questionnaire. It includes 14 questions, from that raw score were calculated and the raw scores were converted to the percentage. Based on the percentage obtained QOL was

categorized into Good(>70%),Satisfactory(40 to 70%),and Poor(<40%). Based on the results, it was found that "Good" QOL was shown by patients in the age group 30-45.

In the Fluoxetine group, 4.8% female were having poor QOL, 57.1% with satisfactory QOL and 38.1% with Good QOL. Among males, 14.3% were having poor QOL, 35.7% with satisfactory QOL and 50% with good QOL. In the escitalopram group, 5% female were having poor QOL, 45% with satisfactory QOL and 50% with Good QOL. Among males, 6.7% were having poor QOL, 33.3% with satisfactory QOL and 60% with good QOL.

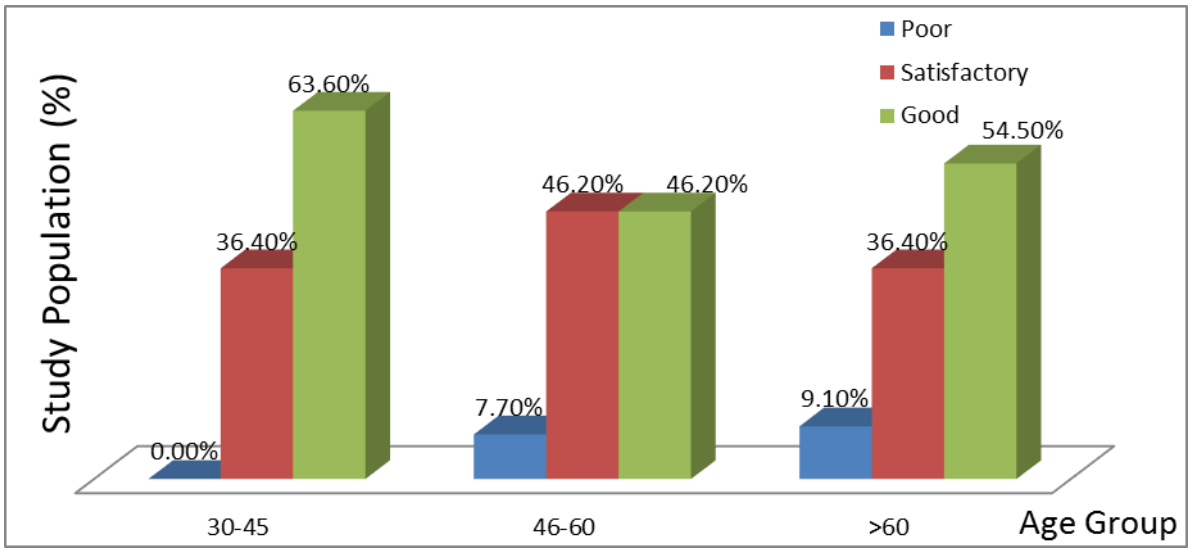

Figure 6: Frequency distribution of patients based on QOL and age group (Escitalopram)

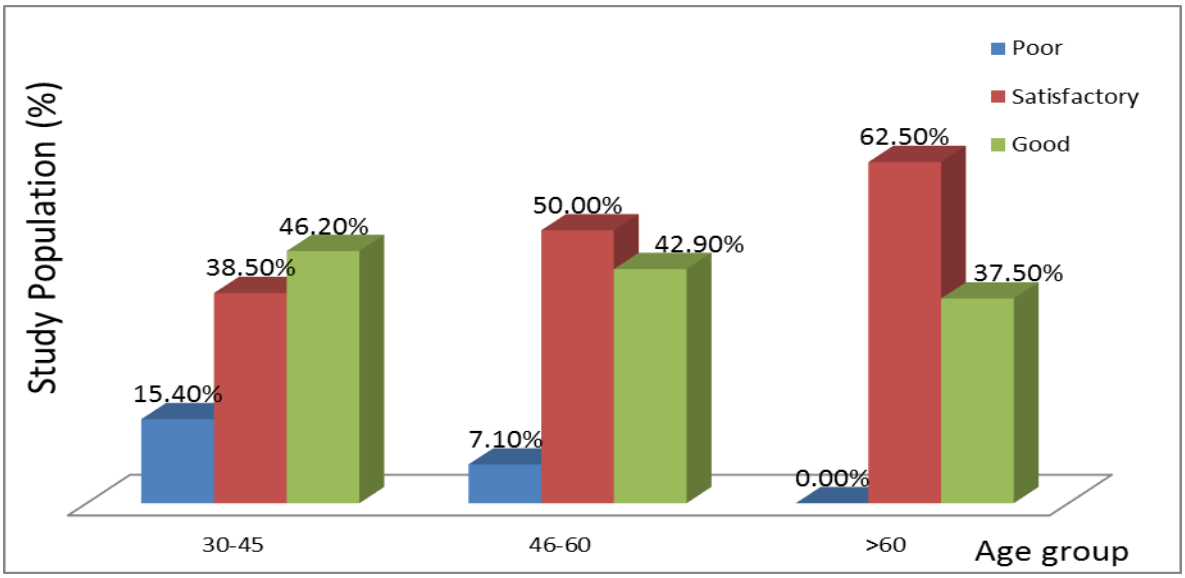

Figure 7: Frequency distribution of patients based on QOL and age group (Fluoxetine)

CONCLUSION

From the above results, it can be inferred that the use of Escitalopram can reduce the chance of cardiovascular events by reducing the CRP levels and FBS than Fluoxetine and the results were statistically significant ($p<0.05$) using the paired t-test. The QOL was found to be Good in 54.29%, 42.86 % of the patient receiving Escitalopram and Fluoxetine respectively. Thus, Escitalopram may be considered as the treatment of choice in patients with comorbid Type 2 Diabetes.

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